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Alternative Natural Management of Dyslipidemia

Abdullah Glil Alkushi

Abstract

In hypercholesterolemic patients, besides therapeutic treatments, alternative treatments can be used such as lifestyle changes, e.g. avoiding smoking, regular exercise, and consuming a diet rich in fiber and low in trans saturated and saturated fats. There are also certain plant products, such as the gum residue guggulipid, that are used in India as a traditional medicine to reduce blood cholesterol levels. Similarly, red yeast rice and rice bran oil have been observed to reduce elevated cholesterol levels. Other herbal products have also been investigated for their role in lowering cholesterol levels, as well as various other herbs and spices such as ginger and turmeric. Another herbal remedy available for reducing high cholesterol levels is the leaf extract of *Cynara scolymus*, commonly known as artichoke thistle. *Cynara cardunculus* var. *scolymus*, or globe artichoke, is mainly cultivated as a food crop. It has an important effect on reducing plasma cholesterol and low-density lipoprotein levels.

Keywords: alternative medicine, lifestyle changes, natural plants, Chinese medicine, vitamins and minerals

1. Dyslipidemia and Lifestyle

Hypercholesterolemia (HC) is defined as the increase in the levels of cholesterol in the blood. As per the recommendation of the expert panel of the National Cholesterol Education Program, desirable blood cholesterol levels should be <200 mg/dL. Levels ranging between 200 and 239 mg/dL are considered as borderline for cholesterol levels, and individuals with blood cholesterol levels above 240 mg/dL are considered hypercholesterolemic [1]. HC occurs due to both environmental and genetic factors [2]. According to familial HC, environmental factors mainly include obesity and diets rich in saturated fats, whereas genetic factors comprise the additive effects of several genes or defects in a single gene [3–5]. Elevated cholesterol levels in the blood not only cause coronary heart disease but can also lead to stroke and damage to the brain [6, 7]. High cholesterol has also been linked to peripheral vascular disease, in which fat is deposited mainly in the arteries that lead to the legs and feet [8]. HC is also linked to type 2 diabetes and hypertension [9, 10].

In hypercholesterolemic patients, besides therapeutic treatments, alternative treatments can be used such as lifestyle changes, e.g. avoiding smoking, regular exercise, and consuming a diet high in fiber and low in trans saturated and saturated fats. Similarly, red yeast rice and rice bran oil have been observed to reduce elevated cholesterol levels. Other herbal products have also been investigated for their role in lowering cholesterol levels, as well as various other herbs and spices such as ginger and turmeric.

Another herbal remedy is the leaf extract of *Cynara scolymus*, commonly known as artichoke thistle. *Cynara cardunculus* var. *scolymus*, or globe artichoke, is mainly cultivated as a food crop. It has important effects in reducing plasma cholesterol and low-density lipoprotein (LDL) levels. Also, many vitamins and minerals help to reduce and control fat and cholesterol levels.

These will be discussed in this chapter.

1.1 Lifestyle changes

One of the most important things in the natural treatments of dyslipidemia is to reduce body weight and take regular exercise [11], which will help to regulate blood cholesterol [12] and decrease the high risk of developing cardiovascular diseases, especially coronary heart disease [13].

1.2 Stopping smoking

This is important in controlling high blood cholesterol, decreasing the risk of coronary heart disease, and improving high-density lipoprotein (HDL) cholesterol [14]. The mechanism of cigarette smoking will have an effect on lipid profile and enhance oxidation of plasma LDL, which leads to endothelial function impairment.

1.3 Alcohol intake

Alcohol has adverse effects on cholesterol and lipid levels, including raising serum triglyceride and HDL cholesterol levels. It has a minimum effect on LDL cholesterol but has effects on the body, including hepatic toxicity, cardiomyopathy, impaired reflexes, and psychosocial problems [15].

1.4 Exercise

Exercise is important in reducing the chance of developing heart disease. It is also important to reduce body weight, which can lead to reduced levels of fat and cholesterol [11].

Physical activity and exercise can be an important factor to improve cholesterol levels, increase HDL, and reduce LDL and triglycerides [16].

Aerobic exercise can generally improve lipid profile [17].

Moderate intensity aerobic exercise and an increase in physical activity in healthy people for more than 30 minutes for 5 days a week are important to maintain low LDL, cholesterol, and triglyceride levels, as well as increase HDL levels [18, 19].

In dyslipidemia especially in older or disabled individuals, increasing physical activity for more than 30 minutes for 5 days a week, moderate-intensity aerobic exercise [19], and high-intensity resistance exercises can all reduce LDL and triglycerides and increase HDL [20].

The beneficial effects of regular physical activity and exercise on cholesterol levels are important in the management of dyslipidemia and can lead to reducing the risks of heart attacks, strokes, and coronary heart disease.

2. Food that should be avoided

1. Food containing too much sugar and carbohydrates, which stimulate the liver to produce more cholesterol, should be avoided.

2. Hydrogenated and trans fats increase cholesterol and the risk of cardiovascular diseases.
3. Red meat and animal products increase the risk of dyslipidemia.

3. Food and dyslipidemia

Foods that help to decrease dyslipidemia are shown in **Tables 1** and **2**.

3.1 Dietary fiber intake

Dietary fiber (DF) intake provides many health benefits. However, the average fiber intake for US children and adults is less than half of the recommended levels. Individuals with high intakes of DF appear to be at significantly lower risk for developing coronary heart disease, stroke, hypertension, diabetes, obesity, and certain gastrointestinal diseases. Increasing fiber intake lowers blood pressure and serum cholesterol levels.

The effect of dietary soluble fiber on serum cholesterol levels has been extensively documented and promoted. The main mechanisms for the cholesterol-lowering effects of water-soluble and -insoluble DFs include binding and excretion of bile acids (BAs) in the small intestine. The cholesterol-reducing effect of water-insoluble DF, such as lignin or citric fiber, is rather low compared to water-soluble DF and is mainly based on direct binding of BAs. In the small intestine the BAs are bound to the insoluble DF and excreted from the enterohepatic circulation together with the undigested DF, which results in a lowering of blood cholesterol levels.

In addition, soluble fibers are known to bind to BAs in the small intestine, thereby removing them from the body and reducing the rate of BA recycling. The loss of BAs in the stool stimulates the liver to increase cholesterol uptake from the circulation to replenish the BA supply. As a result, concentrations of serum total and LDL cholesterol are reduced, while HDL cholesterol and triglycerides are generally unaffected [21].

3.2 Omega-3

Omega-3 fatty acids are presented in two formulas:

- Docosahexaenoic acid (DHA)
- Eicosapentaenoic acid (EPA)

Omega-3 fatty acids are important in reducing triglycerides and non-HDL cholesterol [22–24].

Reducing triglycerides and cholesterol helps to reduce atherosclerosis [25–28].

Using omega-3 fatty acids has benefits in metabolic abnormality associated with non-alcoholic fatty liver in patients with hyperlipidemia [29].

3.3 Garlic

Garlic (*Allium sativum*) belongs to onion genes. It used as an herb medication for various diseases. It has major roles in decreasing risk factors of cardiovascular diseases like high blood pressure and high serum lipids [30–33].

Plant name	Type	Effects on lipid profile
Dietary fiber	Food	Lowers LDL and cholesterol levels
Omega-3	Food	Lowers cholesterol and triglyceride levels
Garlic	Food	Lowers cholesterol and triglyceride levels
Red yeast rice	Food	Lowers cholesterol level
Chinese medicine	Herbal	Lowers hyperlipidemia
Artichoke	Food	Lowers cholesterol level
Fenugreek	Herbal	Lowers cholesterol level
Gum residue guggulipid	Herbal	Lowers LDL and cholesterol levels
Ginger	Food	Lowers cholesterol level

Table 1.
Foods and herbals and their effects on lipid profiles.

Name	Type	Effects on lipid profile
Vitamin B3 (niacin)	Water-soluble vitamin	Lowers LDL, cholesterol, and triglyceride levels
Vitamin B5	Water-soluble vitamin	Lowers LDL, cholesterol, and triglyceride levels
Vitamin C	Water-soluble vitamin	Protects against LDL oxidation
Vitamin D	Fat-soluble vitamin	Reduces the risk of arterial blockage
Magnesium	Mineral	Protects against LDL oxidation
Manganese	Mineral	Protects against LDL oxidation
Zinc	Mineral	Protects against dangerous lipoproteins and promotes HDL
Selenium	Mineral	Protects against dangerous lipoproteins
Copper	Mineral	Protects against dangerous lipoproteins
Coenzyme Q10	Mineral	Protects against dangerous lipoproteins
Chromium	Mineral	Increases HDL level
Choline	Mineral	Controls HDL level
Inositol	Mineral	Lowers LDL and triglyceride levels
Lipoic acid	Mineral	Lowers LDL and protects against cholesterol oxidation
Carnitine	Mineral	Lowers LDL and triglyceride levels

Table 2.
Vitamins and minerals and their effects on lipid profiles.

Garlic reduces cholesterol, LDL, and triglyceride levels by inhibiting cholesterol biosynthesis in the liver and LDL oxidation [34–38].

There are a few side effects associated with using garlic such as allergic dermatitis [39] and its interference with oral anticoagulant drugs [39].

3.4 Red yeast rice

Red yeast rice is a product of rice and is found in China and many Asian countries where it is used as a traditional medicine [40, 41].

Biochemically it contains polyketides, unsaturated fatty acids, phytosterols, pigments, and monacolins [41, 42]. It lowers cholesterol by inhibiting 5-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the rate-limiting step for cholesterol synthesis in the liver. This component, especially monacolins, is chemically similar to lovastatin (a drug used to treat hypercholesterolemia) [41, 43].

3.5 Chinese medicine

Traditional Chinese medicine (TCM) has been used in clinical practice for many centuries. Chinese medicine has shown good effects for human health and treating many diseases. Recently, TCM has shown a beneficial effect for treating dyslipidemia; however, its mechanism remains unclear or totally unknown. Many studies on dyslipidemia with a single Chinese herb showed that TCM can improve phlegm, dampness, and blood stasis syndromes in patients with hyperlipidemia, therefore it has a beneficial effect for lowering hyperlipidemia monomers or effective extracts [44–46].

One study [46] showed that Chinese herbs, which have effects on hyperlipidemia, have four beneficial characteristics:

1. Clearing heat and removing toxicity, for example, Radix et Rhizoma Rhei, Rhizoma Polygoni Cuspidati, Semen Cassia, Coptis chinensis, Scutellaria baicalensis, Gynostemma pentaphyllum, and Radix Puerariae.
2. Promoting blood circulation and removing blood stasis, for example, Fructus crataegi, red yeast rice, Rhizoma, Radix *Salvia miltiorrhizae*, and Turmerone.
3. Eliminating dampness and phlegm, for example, Rhizoma Alismatis, plantain seed, and folium nelumbinis.
4. Increasing body energy, for example, Radix Astragali, Radix Ginseng, and Radix polygoni multiflori.

3.6 Artichoke

Another herbal remedy available for reducing high cholesterol levels is the leaf extract of *Cynara scolymus*, commonly known as artichoke thistle. *Cynara cardunculus* var. *scolymus*, or globe artichoke, is mainly cultivated as a food crop. It is a perennial plant that is largely native to the Mediterranean region in Southern Europe and Northern Africa, and the Canary Islands. In addition to food, artichoke is used in tea and liqueur preparation. Studies on the medicinal properties of artichoke have been continuing over the last six decades. Several in vitro and in vivo studies have investigated the effect of artichoke leaf extract (ALE), especially cymarine, in reducing plasma cholesterol levels [47–50]. Along with cymarine, the antiatherosclerotic effect of luteolin-rich artichoke extract reduces LDL oxidation in a dose-dependent manner [51]. A dose-dependent inhibition of cholesterol biosynthesis, using ALE, was also shown in primary-cultured rat hepatocytes [52].

In addition to in vitro and in vivo studies, randomized controlled studies have assessed the effects of the oral administration of ALE in hypercholesterolemic patients. Bundy et al. assessed the effect of ALE on plasma lipid levels and general well-being in healthy individuals with mild to moderate HC [53]. The participants of the study received 1280 mg of ALE daily (four tablets of 320 mg) for 12 weeks. The majority of participants were females, and almost 90% of them were more than 40 years old. The plasma cholesterol levels were found to be reduced by 4.2%

in the group administered ALE, whereas they increased by 1.9% in the placebo group. No significant difference in LDL cholesterol, HDL cholesterol, or triglycerides was observed between the groups. Englisch et al. conducted a similar study among 18–70-year-old hypercholesterolemic patients [54]. In addition to treatment with cholesterol-reducing drugs, participants were prohibited from antibiotic treatment. The intervention group received 1800 mg of ALE for 6 weeks. Total cholesterol levels were reduced by 18.5% in the group administered with ALE as compared to a 8.6% reduction in the placebo group. In addition to atherosclerosis, HC can affect organs such as kidneys. Studies in rats have shown that cholesterol can increase the incidence of glomerulosclerosis, and in vitro cell culture studies using human glomerular cells revealed the possible mechanisms that are involved in lipid-influenced glomerular damage [55]. Another study showed that treating HC in obese rats reduced their glomerular injuries [56]. Similar observations have also been made in studies with humans. Individuals with high triglycerides or a lecithin–cholesterol acyltransferase deficiency gradually developed renal failure due to glomerulosclerosis [57].

C. cardunculus leaf extract (CCL) not only has cholesterol-reducing capacity but also reduces blood glucose levels and repairs impaired kidney function and damage. These findings are significant particularly because HC results in further complications such as diabetes and kidney damage, both of which can be treated effectively with artichoke [50].

The hypercholesterolemic properties of artichoke involve inhibition of the enzyme HMG-CoA reductase. By lowering blood cholesterol levels and improving lipid profile, experts believe that artichoke can reduce the risks of arteriosclerosis and coronary heart disease and found that both CCL and *C. cardunculus* pulp extract.

decrease the concentration of the respective enzymes (an increase in levels of aspartate transaminase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) are indicators of liver dysfunction), hence serving hepatoprotective and regenerating effects [58]. Thus, it was concluded that artichoke has a beneficial effect on cardiovascular and liver disease.

3.7 Fenugreek seeds

Fenugreek (*Trigonella foenumgraecum*) has an effect on cholesterol and blood sugar. It is a good source of dietary fiber and has beneficial effects on decreasing cholesterol levels in blood and the liver [59, 60].

The mechanism of the lipid-lowering effect of fenugreek seeds is due to the presence of 4-hydroxyisoleucine, a branched chain amino acid [61], and its action on adipocytes and liver cells, which leads to decreased triglycerides, cholesterol, and LDL [62, 63].

3.8 Gum residue guggulipid

A gum resin of the tree *Commiphora mukul*, used for the management of obesity and lipid disorders, is centuries old [64]. The extract of this gum resin, designated guggulipid, has lipid-lowering effects in normal and hyperlipidemic animals (rats, rabbits, and monkeys) [65, 66].

In humans, many studies of the effect of gum resin gumsome in response to guggul treatment were observed in of patients in India [67].

In the United States, studies showed that 18% of patients showed a response to guggulipid treatment, with a decrease in LDL levels of more than 5% [68].

Variations in the results of clinical studies are due to many factors such as ethnic and genetic backgrounds, dietary restraints, and lifestyle [69].

3.9 Ginger

Ginger (*Zingiber officinale*) is a traditional natural plant, which has many characteristics such as decreasing lipid levels, antiplatelet aggregation, and antioxidant and anticarcinogenic qualities [70]. Several studies show that ginger can lower high cholesterol levels in animals. In humans a few study results showed the effects of using ginger in patients with high cholesterol and in the treatment of dyslipidemia [71].

4. Vitamins and minerals

4.1 Vitamin B3 (niacin)

Niacin is a water-soluble vitamin. It effectively lowers the atherogenic lipoprotein(a) by decreasing the rate of synthesis in the liver and lowering the level of cholesterol as well as triglycerides [72, 73]. It is important in reducing the incidence of cardiovascular disease.

4.2 Vitamin B5

Vitamin B5 is a water-soluble vitamin, which is also called pantothenic acid. It is important in the synthesis of coenzyme A, as well as lowering LDL metabolism and reducing triglycerides [74, 75].

4.3 Vitamin C

Vitamin C is a water-soluble vitamin and is essential for repairing tissues and enzyme production. It has a role in lipid metabolism, protects LDL from oxidation, and lowers atherosclerosis and lipoprotein(a) in some people [76, 77].

4.4 Vitamin D

Vitamin D is a fat-soluble vitamin and has an important function in the body, including calcium homeostasis and suppressing foam cell formation, which reduces the risk of arterial blockage [78, 79] therefore reducing cardiovascular disease problems.

4.5 Magnesium

Magnesium protects LDL from being oxidized [80, 81].

4.6 Manganese

Manganese is a cofactor to the antioxidant superoxide dismutase that repairs damage to blood vessels caused by oxidized LDL [82, 83].

4.7 Zinc

Zinc protects against dangerous lipoproteins that lead to vascular inflammation and plaque formation. It also controls the gene that makes HDL [84, 85].

4.8 Selenium

Selenium prevents postprandial change in lipoproteins, which makes them easy to oxidize and become harmful [86, 87].

4.9 Copper

Many copper-dependent enzymes affect lipoprotein metabolism that build up fats and cholesterol in arteries [88–90].

4.10 Coenzyme Q10

Coenzyme Q10 lowers lipoprotein(a) and improves dyslipidemia medicine [91, 92].

4.11 Chromium

Chromium increases HDL levels and cooperates with niacin (B3) for dyslipidemia [93–95].

4.12 Choline

Choline controls HDL metabolism due to the enzyme lecithin cholesterol acyltransferase that has beneficial effects on lipoprotein metabolism [96, 97].

4.13 Inositol

Inositol lowers LDL levels, especially in patients with metabolic syndrome. It also lowers triglyceride levels [98–100].

4.14 Lipoic acid

Lipoic acid lowers LDL levels and protects against oxidized cholesterol [101, 102].

4.15 Carnitine

Carnitine lowers triglycerides, LDL, and the atherogenic lipoprotein(a) by transporting fatty acids into cells so that they can be used as energy [103–105].

5. Conclusion

Besides pharmacological treatments for HC, using alternative treatments may help to increase the effectiveness of drugs. Alternative treatments can help to alter sedentary lifestyles and include exercise, stopping smoking, and eating a number of foods (omega-3, garlic, red yeast rice), herbs (Chinese medicine), vitamins (B, B5, C, and D), and many minerals.

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References

- [1] Goodman DS, Hulley SB, Clark LT, et al. expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. The expert panel. *Archives of Internal Medicine*. 1988;**148**:36-69
- [2] Bhatnagar D, Soran H, Durrington PN. Hypercholesterolaemia and its management. *BMJ*. 2008;**337**:a993
- [3] Innerarity TL, Mahley RW, Weisgraber KH, Bersot TP, Krauss RM, Vega GL, et al. Familial defective apolipoprotein B-100: A mutation of apolipoprotein B that causes hypercholesterolemia. *Journal of Lipid Research*. 1990;**31**:1337-1349
- [4] Grundy SM. George Lyman Duff Memorial Lecture. Multifactorial etiology of hypercholesterolemia. Implications for prevention of coronary heart disease. *Arteriosclerosis and Thrombosis*. 1991;**11**:1619-1635
- [5] Sniderman AD, Tsimikas S, Fazio S. The severe hypercholesterolemia phenotype: Clinical diagnosis, management, and emerging therapies. *Journal of the American College of Cardiology*. 2014;**63**:1935-1947
- [6] Clark LT. Cholesterol and heart disease: Current concepts in pathogenesis and treatment. *Journal of the National Medical Association*. 1986;**78**:743-751
- [7] Navi BB, Segal AZ. The role of cholesterol and statins in stroke. *Current Cardiology Reports*. 2009;**11**:4-11
- [8] Cooke JP. The pathophysiology of peripheral arterial disease: Rational targets for drug intervention. *Vascular Medicine*. 1997;**2**:227-230
- [9] Kwiterovich PO. Primary and secondary disorders of lipid metabolism in pediatrics. *Pediatric Endocrinology Reviews*. 2008;**5**(Suppl 2):727-738
- [10] Ivanovic B, Tadic M. Hypercholesterolemia and hypertension: Two sides of the same coin. *American Journal of Cardiovascular Drugs*. 2015;**15**:403-414
- [11] National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). Bethesda, Md: National Cholesterol Education Program, National Institutes of Health, National Heart, Lung, and Blood Institute; 1993. DHSS Publication No. (NIH) 93-3095:5
- [12] Yeshurun D, Gotto AM Jr. Hyperlipidemia: Perspectives in diagnosis and treatment. *Southern Medical Journal*. 1995;**88**:379-391
- [13] The lipid research clinics coronary primary prevention trial results. I. Reduction in incidence of coronary heart disease. *Lipid Research Clinics Program*. *JAMA*. 1984;**251**:351-364
- [14] Adam D, Gepner M, Megan E. Effect of smoking and smoking cessation on lipid and lipoprotein: Outcomes from a randomized clinical trial. *American Heart Journal*. 2011;**161**(1):145-151
- [15] Ahmed SM, Clasen ME, Donnelly JF. Management of dyslipidemia in adults. *American Family Physician*. 1998;**57**(9):2192-2204
- [16] Ferguson MA, Alderson NL, Trost SG, et al. Effects of four different single exercise sessions on lipids, lipoproteins, and lipoprotein lipase. *Journal of Applied Physiology*. 1998;**85**(3):1169-1174
- [17] Kraus W, Houmard J, Duscha B, et al. Effects of the amount and intensity

of exercise on plasma lipoproteins. *The New England Journal of Medicine*. 2002;**347**(19):1483-1492

[18] Aadahl M, Kjaer M, Jørgensen T. Associations between overall physical activity level and cardiovascular risk factors in an adult population. *European Journal of Epidemiology*. 2007;**22**(6):369-378

[19] Fett C, Fett W, Marchini J. Circuit weight training vs jogging in metabolic risk factors of overweight/obese women. *Arquivos Brasileiros de Cardiologia*. 2009;**93**(5):519-525

[20] Lira F, Yamashita A, Uchida M, et al. Low and moderate, rather than high intensity strength exercise induces benefit regarding plasma lipid profile. *Diabetology and Metabolic Syndrome*. 2010;**2**:31

[21] Osfor MMH, Ashsh AM, ElSawy NA, Qusty NFH, Alkushi AG. Effect of wheat bran consumption on serum lipid profile of hypercholesterolemia patients residence in Holly Makah. *Asian Journal of Natural & Applied Sciences*. 2016;**5**(1):1-9

[22] Harris WS, Ginsberg HN, Arunakul N, et al. Safety and efficacy of Omacor in severe hypertriglyceridemia. *Journal of Cardiovascular Risk*. 1997;**4**(5-6):385-391

[23] Pownall HJ, Brauchi D, Kilinc C, et al. Correlation of serum triglyceride and its reduction by omega-3 fatty acids with lipid transfer activity and the neutral lipid compositions of high-density and low-density lipoproteins. *Atherosclerosis*. 1999;**143**(2):285-297

[24] Maki KC, Orloff DG, Nicholls SJ, et al. A highly bioavailable omega-3 free fatty acid formulation improves the cardiovascular risk profile in high-risk, statin-treated patients with residual hypertriglyceridemia (the ESPRIT trial). *Clinical Therapeutics*. 2013;**35**(9):1400-1411

[25] Jorgensen AB, Frikke-Schmidt R, Nordestgaard BG, et al. Loss-of-function mutations in APOC3 and risk of ischemic vascular disease. *The New England Journal of Medicine*. 2014;**371**(1):32-41

[26] TG and HDL Working Group of the Exome. Sequencing Project NHLaBI. Loss-of-function mutations in APOC3, triglycerides, and coronary disease. *The New England Journal of Medicine*. 2014;**371**(1):22-31

[27] Khetarpal SA, Rader DJ. Triglyceride-rich lipoproteins and coronary artery disease risk: New insights from human genetics. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2015;**35**(2):e3-e9

[28] Dewey FE, Gusarova V, O'Dushlaine C, et al. Inactivating variants in ANGPTL4 and risk of coronary artery disease. *The New England Journal of Medicine*. 2016;**374**(12):1123-1133

[29] Qin Y, Zhou Y, Chen S-H, et al. Fish oil supplements lower serum lipids and glucose in correlation with a reduction in plasma fibroblast growth factor 21 and prostaglandin E2 in nonalcoholic fatty liver disease associated with hyperlipidemia: A randomized clinical trial. *PLoS One*. 2015;**10**(7):e0133496. DOI: 10.1371/journal.pone.0133496. Herder C, editor

[30] Ackermann RT, Mulrow CD, Ramirez G. Garlic shows promise for improving some cardiovascular risk factors. *Archives of Internal Medicine*. 2001;**161**(6):813

[31] Qidwai W, Ashfaq T. Role of garlic usage in cardiovascular disease prevention: An evidence-based approach. *Evidence-Based Complementary and Alternative Medicine*. 2013;**2013**:1-9. Article ID 125649

[32] Khoo YSK, Aziz Z. Garlic supplementation and serum cholesterol:

A meta-analysis. *Journal of Clinical Pharmacy and Therapeutics*. 2009;**34**(2):133-145

[33] Osamor PE, Owumi BE. Complementary and alternative medicine in the management of hypertension in an urban Nigerian community. *BMC Complementary and Alternative Medicine*. 2010;**10**(1):36

[34] Zhang XH, Lowe D, Giles P. A randomized trial of the effects of garlic oil upon coronary heart disease risk factors in trained male runners. *Blood Coagulation & Fibrinolysis*. 2001;**12**(1):67-74

[35] Lau BHS. Suppression of LDL oxidation by garlic compounds is a possible mechanism of cardiovascular health benefit. *The Journal of Nutrition*. 2006;**136**(3):765-768

[36] Duda G, Suliburska J, Pupek-Musialik D. Effects of short-term garlic supplementation on lipid metabolism and antioxidant status in hypertensive adults. *Pharmacological Reports*. 2008;**60**(2):163

[37] Zeng T, Zhang CL, Zhao XL. The roles of garlic on the lipid parameters: A systematic review of the literature. *Critical Reviews in Food Science and Nutrition*. 2013;**53**(3):215-230

[38] Jahan F, Nanjib K, Qidwai W. Role of garlic in dyslipidemia: An evidence based review. *Scientific Journal of Biological Sciences*. 2015;**4**(5):36-42

[39] Steiner M, Khan AH, Holbert D, Lin RI. A double-blind crossover study in moderately hypercholesterolaemic men that compared the effect of aged garlic extract and placebo administration on blood lipids. *The American Journal of Clinical Nutrition*. 1996;**64**:866-870

[40] Burke FM. Red yeast rice for the treatment of dyslipidemia. *Current Atherosclerosis Reports*. 2015;**17**(4):495

[41] Francini-Pesenti F et al. Red yeast rice in the long-term treatment of hypercholesterolemia. A single-center experience. *Acta Scientific Agriculture*. 2017;**1**(3):16-18

[42] Patel S. Functional food red yeast rice (RYR) for metabolic syndrome amelioration: A review on pros and cons. *World Journal of Microbiology and Biotechnology*. 2016;**32**(5):2035-2042

[43] Zhang Z et al. Cytotoxic monacolins from red yeast rice, a Chinese medicine and food. *Food Chemistry*. 2016;**202**:262-268

[44] Shi HX, Li QH. Research progress of traditional Chinese medicine treatment of hyperlipidemia. *Journal of Medical Forum*. 2007;**28**(10):123-124

[45] Jiang JG. The clinical study progress of Chinese herbal medicine for hyperlipidemia. *Journal of Practical Traditional Chinese Medicine*. 2008;**24**(9):614-615

[46] Guo M, Liu Y, Gao ZY, Shi DZ. Chinese herbal medicine on dyslipidemia: Progress and perspective. *Evidence-based Complementary and Alternative Medicine*. 2014;**2014**:1-11

[47] Wojcicki J, Winter S. Effect of preparation Cynarex on the blood serum lipids level of the workers exposed to the chronic action of carbon disulphide. *Medycyna Pracy*. 1975;**26**:213-217

[48] Wójcicki J. Effect of 1,5-dicaffeoylquinic acid (cynarine) on cholesterol levels in serum and liver of acute ethanol-treated rats. *Drug and Alcohol Dependence*. 1978;**3**:143-145

[49] Wojcicki J, Samochowiec L, Kosmider K. Influence of an extract from artichoke (*Cynara scolymus* L.) on the level of lipids in serum of aged men. *Herba Polonica*. 1981;**27**:265-268

- [50] Alkushi AG. Biological effect of *Cynara cardunculus* on kidney status of hypercholesterolemic rats. *Pharmacognosy Magazine*. 2017;**13**:S430-S436
- [51] Brown JE, Rice-Evans CA. Luteolin-rich artichoke extract protects low density lipoprotein from oxidation in vitro. *Free Radical Research*. 1998;**29**:247-255
- [52] Gebhardt R. Inhibition of cholesterol biosynthesis in primary cultured rat hepatocytes by artichoke (*Cynara scolymus* L.) extracts. *The Journal of Pharmacology and Experimental Therapeutics*. 1998;**286**:1122-1128
- [53] Bundy R, Walker AF, Middleton RW, Wallis C, Simpson HC. Artichoke leaf extract (*Cynara scolymus*) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: A randomized, double blind placebo controlled trial. *Phytomedicine*. 2008;**15**:668-675
- [54] Englisch W, Beckers C, Unkauf M, Ruepp M, Zinserling V. Efficacy of artichoke dry extract in patients with hyperlipoproteinemia. *Arzneimittel-Forschung*. 2000;**50**:260-265
- [55] Gröne EF, Walli AK, Gröne HJ, Miller B, Seidel D. The role of lipids in nephrosclerosis and glomerulosclerosis. *Atherosclerosis*. 1994;**107**:1-13
- [56] Kasiske BL, O'Donnell MP, Cleary MP, Keane WF. Treatment of hyperlipidemia reduces glomerular injury in obese Zucker rats. *Kidney International*. 1988;**33**:667-672
- [57] Samuelsson O, Mulec H, Knight-Gibson C, Attman PO, Kron B, Larsson R, et al. Lipoprotein abnormalities are associated with increased rate of progression of human chronic renal insufficiency. *Nephrology, Dialysis, Transplantation*. 1997;**12**:1908-1915
- [58] Header EA, ElSawy NA, Alkushi AG. Biological effect of *Cynara cardunculus* on liver and heart status for hypercholesterolemic rats. *Australian Journal of Basic and Applied Sciences*. 2017;**11**(2):41-49
- [59] Nadkarni KM. *Trigonella foenum graecum*: Indian materia. *Médica*. 1993;**1240**:1249
- [60] Kumar K, Kumar S, Datta A, Bandyopadhyay A. Effect of fenugreek seeds on glycemia and dyslipidemia in patients with type 2 diabetes mellitus. *International Journal of Medical Science and Public Health*. 2015;**4**(7):997-1000
- [61] Belaid Nouria Y, Bakhta H, Bouaziz M. Study on the lipid profile and the parieto-temporal lipid peroxidation in $AlCl_3$ mediated neurotoxicity: the modulatory effect of the fenugreek seeds. *Lipids in Health and Disease*. 2012;**11**:6
- [62] Jetle L, Harvey L, Eugeni K, Leven SN. The 4-hydroxy isoleucine plant-derived treatment for metabolic syndrome. Current opinion treatment for the metabolic syndrome. *Current Opinion in Investigational Drugs*. 2000;**10**:353-358
- [63] Sharma MS, Choudhary PR. Hypolipidemic effect of fenugreek seeds and its comparison with atorvastatin on experimentally induced hyperlipidemia. *Journal of the College of Physicians and Surgeons—Pakistan*. 2014;**24**(8):539-542
- [64] Dev S. Ethnotherapeutics and modern drug development. The potential of Ayurveda. *Current Science*. 1997;**73**:909-928
- [65] Satyavati GV. Gum guggul (*Commiphora mukul*)—The success story of an ancient insight leading to a modern discovery. *The Indian Journal of Medical Research*. 1988;**87**:327-335

- [66] Singh K, Chander R, Kapoor NK. Stimulation of low density lipoprotein receptor activity in liver membrane of guggulsterone treated rats. *Pharmacological Research*. 1990;**22**:37-44
- [67] Deng R. Therapeutic effects of guggul and its constituent guggulsterone: Cardiovascular benefits. *Cardiovascular Drug Reviews*. 2007;**25**:375-390
- [68] Szapary PO, Wolfe ML, Bloedon LT, et al. Gugulipid for the treatment of hypercholesterolemia: A randomized controlled trial. *Journal of the American Medical Association*. 2003;**290**:765-772
- [69] Ramachandran C, Nair SM, Quirrin K-W, Melnick SJ. Hypolipidemic effects of a proprietary Commiphora Mukul gum resin extract and medium-chain triglyceride preparation (GU-MCT810). *Journal of Evidence-Based Complementary & Alternative Medicine*. 2013;**18**(4):248-256
- [70] Ellen RL, McPherson R. Long-term efficacy and safety of fenofibrate and a statin in the treatment of combined hyperlipidemia. *The American Journal of Cardiology*. 1998;**81**:60-65
- [71] Fuhrman B, Rosenblat M, Hayek T, Coleman R, Aviram M. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E-deficient mice. *The Journal of Nutrition*. 2000;**130**:1124-1131
- [72] Seed M, O'Connor B, Perombelon N, et al. The effects of nicotinic acid and acipimox on lipoprotein (a) concentration and turnover. *Atherosclerosis*. 1993;**101**:61-68
- [73] Kostner K, Gupta S. Niacin: A lipid polypill? *Expert Opinion on Pharmacotherapy*. 2008;**9**:2911-2920
- [74] McRae M. Treatment of hyperlipoproteinemia with pantethine: A review and analysis of efficacy and tolerability. *Nutrition Research*. 2005;**25**:319-333
- [75] Rumberger J, Napolitano J, Azmumano I, et al. Pantethine, a derivative of vitamin B(5) used as a nutritional supplement, favorably alters low-density lipoprotein cholesterol metabolism in low- to moderate-cardiovascular risk North American subjects: A triple-blinded placebo and diet-controlled investigation. *Nutrition Research*. 2011;**31**:608-615
- [76] Woollard K, Loryman C, Meredith E, et al. Effects of oral vitamin C on monocyte: Endothelial cell adhesion in healthy subjects. *Biochemical and Biophysical Research Communications*. 2002;**294**:1161-1168
- [77] Shariat S, Mostafavi S, Khakpour F. Antioxidant effects of vitamins C and E on the low density lipoprotein oxidation mediated by myeloperoxidase. *Iranian Biomedical Journal*. 2013;**17**:22-28
- [78] Riek A, Oh J, Bernal-Mizrachi C. Vitamin D regulates macrophage cholesterol metabolism in diabetes. *The Journal of Steroid Biochemistry and Molecular Biology*. 2010;**121**:430-433
- [79] Guasch A, Bulló M, Rabassa A, et al. Plasma vitamin D and parathormone are associated with obesity and atherogenic dyslipidemia: A cross-sectional study. *Cardiovascular Diabetology*. 2012;**11**:149
- [80] Sherer Y, Bitzur R, Cohen H, et al. Mechanisms of action of anti-atherogenic effect of magnesium: Lessons from a mouse model. *Magnesium Research*. 2001;**14**:173-179
- [81] Maier J. Low magnesium and atherosclerosis: An evidence-based link. *Molecular Aspects of Medicine*. 2003;**24**:137-146

- [82] Takabe W, Li R, Ai L, et al. Oxidized low-density lipoprotein-activated c-Jun NH2-terminal kinase regulates manganese superoxide dismutase ubiquitination: Implication for mitochondrial redox status and apoptosis. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2010;**30**:436-441
- [83] Perrotta I, Perrotta E, Sesti S, Cassese M and Mazzulla S, et al. MnSOD expression in human atherosclerotic plaques: An immunohistochemical and ultrastructural study. *Cardiovascular Pathology*. 2013;**22**:428-437. Epub ahead of print
- [84] Wu J, Wu Y, Reaves S, et al. Apolipoprotein A-I gene expression is regulated by cellular zinc status in hep G2 cells. *The American Journal of Physiology*. 1999;**277**:C537-C544
- [85] Shen H, MacDonald R, Bruemmer D, et al. Zinc deficiency alters lipid metabolism in LDL receptor deficient mice treated with rosiglitazone. *The Journal of Nutrition*. 2007;**137**:2339-2345
- [86] Natella F, Fidale M, Tubaro F, et al. Selenium supplementation prevents the increase in atherogenic electronegative LDL (LDL minus) in the postprandial phase. *Nutrition, Metabolism, and Cardiovascular Diseases*. 2007;**17**:649-656
- [87] Kaur H, Bansal M. Studies on scavenger receptors under experimental hypercholesterolemia: Modulation on selenium supplementation. *Biological Trace Element Research*. 2011;**143**:310-319
- [88] Hamilton I, Gilmore W, Strain J. Marginal copper deficiency and atherosclerosis. *Biological Trace Element Research*. 2000;**78**:179-189
- [89] Wildman R, Mao S. Tissue-specific alteration in lipoprotein lipase activity in copper-deficient rats. *Biological Trace Element Research*. 2001;**80**:221-229
- [90] DiSilverstro R, Joesph E, Zhang W, et al. A randomized trial of copper supplementation effects on blood copper enzyme activities and parameters related to cardiovascular health. *Metabolism*. 2012;**61**:1242-1246
- [91] Langsjoen P, Langsjoen A. The clinical use of HMG CoA reductase inhibitors and the associated depletion of coenzyme Q10. A review of animal and human publications. *BioFactors*. 2003;**18**:101-111
- [92] Cicero A, Derosa G, Miconi A, et al. Possible role of ubiquinone in the treatment of massive hypertriglyceridemia resistant to PUFA and fibrates. *Biomedicine & Pharmacotherapy*. 2005;**59**:312-317
- [93] Press R, Geller J, Evans G. The effect of chromium picolinate on serum cholesterol apolipoprotein fractions in human subjects. *The Western Journal of Medicine*. 1990;**152**:41-45
- [94] Sealls W, Penque B, Elmendorf J. Evidence that chromium modulates cellular cholesterol homeostasis and ABCA1 functionality impaired by hyperinsulinemia—Brief report. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2011;**31**:1139-1140
- [95] Sundaram B, Singhal K, Sandhir R. Anti-atherogenic effect of chromium picolinate in streptozotocin-induced experimental diabetes. *Journal of Diabetes*. 2013;**5**:43-50
- [96] Vance D. Role of phosphatidylcholine biosynthesis in the regulation of lipoprotein homeostasis. *Current Opinion in Lipidology*. 2008;**19**:229-234
- [97] Kunnen S, Van Eck M. Lecithin:cholesterol acyltransferase:

Old friend or foe in atherosclerosis?
Journal of Lipid Research.
2012;**53**:1783-1799

with type 2 diabetes mellitus.
Clinical Therapeutics. 2003;
25(5):1429-1439

[98] Jariwalla R. Inositol hexaphosphate (IP6) as an anti-neoplastic and lipid-lowering agent. *Anticancer Research*. 1999;**19**:3699-3702

[105] Malaguarnera M, Vacante M, Avitabile T, et al. L-Carnitine supplementation reduces oxidized LDL cholesterol in patients with diabetes. *The American Journal of Clinical Nutrition*. 2009;**89**:71-76

[99] Maeba R, Hara H, Ishikawa H, et al. Myo-inositol treatment increases serum plasmalogens and decreases small dense LDL, particularly in hyperlipidemic subjects with metabolic syndrome. *Journal of Nutritional Science and Vitaminology*. 2008;**54**:196-202

[100] Minozzi M, Nordio M, Pajalich R. The combined therapy myo-inositol plus D-chiro-inositol, in a physiological ratio, reduces the cardiovascular risk by improving the lipid profile in PCOS patients. *European Review for Medical and Pharmacological Sciences*. 2013;**17**:537-540

[101] Zhang Y, Han P, Wu N, He B, Lu Y, Li S, et al. Amelioration of lipid abnormalities by α -lipoic acid through antioxidative and anti-inflammatory effects. *Obesity (Silver Spring)*. 2011;**19**(8):1647-1653

[102] Harding S, Rideout T, Jones P. Evidence for using alpha-lipoic acid in reducing lipoprotein and inflammatory related atherosclerotic risk. *Journal of Dietary Supplements*. 2012;**9**:116-127

[103] Sirtori C, Calabresi L, Ferrara S, et al. L-carnitine reduces plasma lipoprotein(a) levels in patients with hyper Lp(a). *Nutrition, Metabolism, and Cardiovascular Diseases*. 2000;**10**:247-251

[104] Derosa G, Cicero AF, Gaddi A, Mugellini A, Ciccarelli L, Fogari R. The effect of L-carnitine on plasma lipoprotein(a) levels in hypercholesterolemic patients